This guidance was written prior to the February 27, 1997 implementation of FDA's Good Guidance Practices, GGP's. It does not create or confer rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both. This guidance will be updated in the next revision to include the standard elements of GGP's.

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GUIDANCE FOR THE ARRANGEMENT AND CONTENT OF A PREMARKET APPROVAL (PMA) APPLICATION FOR AN ENDOSSEOUS IMPLANT FOR PROSTHETIC ATTACHMENT

MAY 16, 1989

U.S. Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Devices and Radiological Health

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PREFACE

This guidance is intended to aid applicants in the preparation of PMAs for endosseous implants for prosthetic attachment. An endosseous implant is defined as "....a device made of a material such as titanium intended to be surgically placed in the bone of the upper or lower jaw arches to provide support for prosthetic devices, such as artificial teeth, and to restore the patient's chewing function". The guidance pertains to both the portion of the implant that is inserted into bone and the abutments that are attached (i.e., support for prosthetic devices, such as artificial teeth). This document also pertains to the manufacturers that market the abutment portion only. The guidance describes the kind of information needed to evaluate the safety and effectiveness of these devices.

Specific examples of application to every variation of endosseous implant on the market is beyond the scope of this document. For example, the mechanical characteristics documented for each implant may vary according to the type of materials and combination of materials used in fabricating the implant. However, the following generalizations can be made to assist manufacturers in understanding how the guidance should be applied to their respective devices. Clinical trials must be conducted with an abutment attached. However, physical variations of the tested abutments will only need engineering data, described in Section IV, to demonstrate safety and effectiveness. Every size of a specific implant design will not need animal or clinical studies. However, the mechanical characteristics of each size may still be needed to document its mechanical strength. Biocompatibility data will not be needed if the biocompatibility of a material used to construct an endosseous implant has been well established. References to published literature will suffice. Surgical grade titanium is an example of a material with a well established data base. Implants that have been found substantially equivalent to devices marketed prior to the enactment of the Medical Device Amendments (May 28, 1976) will not be required to undergo animal studies. However, if specific claims are made about tissue response to the implant, data from histological specimens may be required. Retrospective data may be submitted if it meets the definition of valid scientific evidence in 21 CFR 860.7.

Wherever possible, an application should follow the guidance presented here and provide an explanation of any omission to avoid unnecessary questions from the Center. An example of an omission would be if certain clinical parameters cannot be recorded with a particular type of prosthesis. The submission of PMAs which contain all necessary information will expedite the review and approval of these applications.

An appendix to the guidance provides information regarding patient informed consent and postmarket surveillance. Also available from the Center is the PMA Manual which covers the arrangement and content of a PMA in detail.

If there are any questions or comments concerning this guidance, please contact:

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Telephone (301)427-8185.

I. Cover Page

A. Name and address of applicant

B. Signature of applicant or authorized representative in the United States

C. Classification (generic) name of the device (if applicable)

D. Device trade name

E. Model number of the device (if applicable)

F. Identifying numbers of all INDs (Investigational New Drugs), NDAs (New Drug Application), IDEs (Investigational Device Exemption), PMAs (Premarket Approval Application), PDPs (Product Development Protocol), reclassification petitions, or 510(k)s previously submitted for this device

G. Indications for use

H. Name, address, and establishment number of manufacturing site(s)

I. Date when manufacturing site(s) will be ready for inspection or date of latest FDA inspection

J. Environmental Impact

1. Claim of categorical exclusion

2. If no claim of categorical exclusion, include an environmental assessment

II. Table of Contents

A. Volume and page number of each item referred to in the table of contents

B. Separate sections for nonclinical laboratory studies and clinical investigations involving human subjects

C. In at least one copy, identify any information believed to be trade secret or confidential commercial or financial information. Although identification is required in only one copy, the confidential information must be included in all copies of the PMA. Submit six copies of each original PMA and three copies of each

amendment or supplement. Additional copies may be requested by FDA if needed for advisory panel review.

III. Summary of Safety and Effectiveness

The summary should contain brief statements of the following points and typically would be 10 - 15 pages in length

A. Indications for use

Give a description of the disease or condition that the endosseous implant will treat, prevent, cure, or mitigate. Include the type of prosthesis that will be attached to the implant (i.e., crown, partial or complete dentures), the type of abutment that can be used with this implant, the intended location for implantation in the alveolar ridge, and the amount of buccal and labial bone support (which would also include bone height) needed for each implant.

B. Contraindications for use

Specify any medical condition that could mitigate the success of the implant.

C. Device description

Explain how the device functions. This explanation should include, but not be limited to, any special mechanism used to distribute the forces of occlusion throughout the implant and surrounding bone, how or if bone ingrowth and attachment is attained, how or if gingival attachment is attained, the exact chemical composition of the implant (including coatings) and the potential long-term toxicity, including carcinogenicity, of each ingredient. This would include the abutments that will be attached to the portion of the implant that is inserted into bone.

D. Alternative practices and procedures

Describe any alternative practices or procedures for treating, preventing, curing, or mitigating the condition for which the device is intended.

E. Marketing history of the device

Give a brief description of the foreign and United States marketing history of the device known to the applicant. At a minimum, include a list of all countries in which the device has been marketed and a list of all countries in which the device has been withdrawn from marketing for any reason related to safety and effectiveness of the

device (this would include medical device reports (MDRs) and user complaint files). Include the history of the marketing of the device by the applicant and, if known, the history of the marketing of the device by any other person.

F. Summary of studies

1. Abstracts of any other data, information or report described in the PMA which relates to safety and effectiveness (21 CFR 814.20(b)(8)(ii))

2. Summaries of the results of the nonclinical laboratory studies and clinical investigations which contain the required parameters as detailed in the technical section of this outline (Section VI)

a) Summaries of the nonclinical laboratory studies

(1) parameters and length of study(ies)

(2) number of devices implanted

(3) results of studies

b) Summary of the clinical investigations

(1) patient inclusion and exclusion criteria

(2) study population demographics, including justification for the number of patients required in the study

(3) study period

(4) safety and effectiveness data

(a) a table of all investigators and number of investigational subjects per investigator

(b) brief discussion of protocol

(c) a table specifying the age and sex of each subject in the study and the totals in each treatment group

(d) a list of all claims with a summary of the evidence for each claim (indications for use) cited in the labeling (the results by claim should be given either by combining the results of equivalent types of studies done or by citing the

results of other well done studies separately and then drawing a conclusion)

(e) an assessment of the comparability of treatment groups (e.g., categorized by single tooth, partial or complete denture prosthesis (fixed or removable)) for each relevant baseline variable and certain combinations of these variables (age, risk factors, gingival health, pocket depth, bone resorption, mobility, etc.) by the use of tables, graphical presentations, and other appropriate statistical techniques

(f) statistical and clinical justification for pooling of data from multiple clinical investigators

(g) references on page, table, figure numbers and statistical analyses in the submission on which the clinical summaries are based

(5) Adverse reactions and complications should include a summary table for each type of adverse reaction, side effect, injury, toxicity, including sensitization and long term safety. Detail any additional and/or corrective surgery that was performed. The incidence and severity of each adverse reaction or effect should be specified, a statement included as to whether the applicant considers the adverse reaction or effect to be significant or not, and the degree of morbidity patient was left with after failure (i.e., irreversible bone loss, pathologic entities such as osteomyelitis, long term antibiotic use, psychoneurosis, etc.). The tables should include the age and sex of each subject and the investigator's name, with a reference to the volume and page number in the application and any documents incorporated by reference where the complete data and reports may be found. For each adverse reaction or effect, state how this information is contained in the labeling, e.g. as a contraindication, warning, precaution or adverse effect.

(6) patient discontinuation with a detailed explanation for discontinuation and time of discontinuation

(7) patient complaints

(8) device failures, failure analysis (including detailed morphological analysis), and replacements (i.e., how did it fail, what components failed, what was the nature of the replacement if done, was there another implant inserted?)

(9) results of statistical analysis of the clinical investigations

(10) contraindications and precautions (i.e., handling of implant, type and material composition of the instrumentation, amount of buccal and lingual bone support, bone height, etc.)

(11) other information from the clinical investigations as appropriate, such as study design and method of randomization

G. Conclusions drawn from the studies

1. Discussion of how the data and information in the application constitute valid scientific evidence (21 CFR 860.7)

2. Discussion of data on safety and effectiveness to provide reasonable assurance that the device is safe and effective for its intended use

3. Risk/Benefit analysis (this analysis should take into consideration the use of anesthetics as a risk)

4. Discussion of postapproval studies or surveillance

IV. Device Characteristics and Manufacturing Section

A. Description of the device, including pictorial representations and mechanical drawings that quantify the dimensional characteristics

B. Description of each of the functional components or ingredients of the device if the device consists of more than one physical component or ingredient

1. The exact chemical composition of each material and/or coating. If a coating is applied, the exact chemical composition and crystallographic structure (if applicable) of the coating, after application, should be supplied.

2. The coating thickness, porosity, and method used for applying the coating to the implant

3. The mechanical characteristics (modulus of elasticity, tensile strength, yield strength, etc) of the material used to make the implant.

4. Rationale for the design, with references to relevant literature should be provided. This would include calculations, analyses and justification for the design and material selected.

5. Surface quality should be depicted. Both surface texture and elemental analysis of surface components (i.e. surface impurities), post-sterilization, should be detailed. Such techniques as electron microscopy and infrared spectroscopy are appropriate.

6. Hardness, particularly at the neck of the implant, should be measured. This measurement should be made with the implant in its final form.

7. Compression strength should be measured. The direction of force should be that normally encountered by the implant during occlusion. If the implant system can be constructed or bent in different orientations, extreme orientations should be tested. Fatigue analysis should also be performed in compression. The extreme orientation(s) that is(are) discussed both in 7 and 8 would be considered to be the orientation that would have the abutment positioned furthest out of the vertical axis of the portion of the implant that is inserted into the bone.

8. Bending strength should be measured. This test should apply a moment about the post of the implant (cantilever beam). Fatigue analysis should also be performed in bending. These measurements should also be repeated if the implant system can be constructed or bent in different orientations (extreme orientations should be tested). Refer to 7, above, for a definition of extreme orientations.

9. If a coating is applied, bonding strength should be measured between the implant and the coating.

10. Detail any special preparation or characteristic of the implant that will promote bone attachment, bone ingrowth, and/or gingival attachment

11. Describe any special mechanism (if any) used to distribute, dampen, reduce or otherwise modify load

transfer from prosthesis to implant or from implant to bone.

C. Description of the properties of the device relevant to the treatment, prevention, cure, or mitigation of a condition

D. Description of the principles of operation of the device

E. Description of the methods, facilities, and controls used in the manufacture, processing, packing and storage of the device

1. The location of the manufacturing facility(ies) with the street address and other appropriate directions and the establishment registration number. These facilities would include, but are not limited to, materials supplier and coating applicator.

2. A description of the organization of the firm including assignment of responsibility (see 21 CFR 820.20, 820.25)

3. A description of the physical plant(s) including environmental controls having an effect on the device (see 21 CFR 820.25, 820.40, 820.56) and an enviromental assessment as required by FDA, an enviromental impact statement meeting the requirements of 21 CFR Part 25

4. A description of manufacturing equipment directly involved with production of the device (see 21 CFR 820.60, 820.61)

5. A description of the manufacturing control system for components (see 21 CFR 820.80, 820.81)

6. A description, including a flow chart, of the manufacturing process and quality control procedures including standards for acceptance or rejection (see 21 CFR 820.100, 820.115, 820.116)

a) The manufacturing documentation of the implant unit should include complete manufacturing process specifications, assembly instructions and manufacturing assembly drawings for each stage, from subassembly to final assembly, with full traceability of the product. Similar documentation should be supplied for top assembly stage of any nonimplanted system components.

b) Manufacturing assembly drawings need not duplicate any drawings requested under sections

IV. A. and B. as long as the applicable drawings are referenced. Cross references between mechanical drawings and assembly drawings should be listed if they are not given on the drawings.

7. The details of mixing, forming, casting, curing, including the materials, sources of the materials, and percentage composition of the materials used in the device. Include coating characteristics such as purity, porosity, crystallographic structure, and coating application process.

8. Assessment of the uniformity of the components in the completed devices and the procedures for quality control. This should include metallurgical radiography, chemical composition and associated characteristics of coating, and other appropriate tests.

9. Methods and techniques to assure the proper surface morphology and texture. This type of quality control should be applied to the final product (after sterilization). Methods used should assure that the implant is free of imperfections such as toolmarks, nicks, scratches, cracks, cavities, burrs, and other defects that could impair the implants serviceability. Examples of methods used to assure surface quality were described in IV. B. 8.

10. A description of packaging, sterilization, and labeling controls (see 21 CFR 820.120, 820.121, 820.130)(the applicant must include a description of sterilization procedures including the method of sterilization, validation, and pyrogencity testing and results)

11. A description of holding, distribution, and installation controls (see 21 CFR 820.150, 820.151, 820.152)

12. A description of finished device inspection procedures. This should include microscopic surface analysis, coating purity, and surface impurities.

13. A description and location of device records (see 21 CFR 820.180, 820.181, 820.182, 820.184, 820.185, 820.195, 820.198)

V. Performance Standards

A. Provide adequate information to demonstrate how the device meets section 514 performance standard (give name or standard); justify any deviation

B. Explain any deviation from a voluntary standard (give name of standard)

VI. Technical Sections

A. Results of the nonclinical or laboratory studies

A statement should be included whether each nonclinical study was conducted in compliance with Good Laboratory Practice for Nonclinical Laboratory Studies, 21 CFR Part 58. If not, give a brief statement of the reason for the noncompliance.

1. Animal studies, with an appropriate animal model, are necessary when the implant, which has been found substantially equivalent to pre-Amendments (prior to May 28, 1976) devices by the FDA through premarket notification (510(k)) procedures, has specific claims in labeling about the tissue-implant interface (e.g., osseointegration, periodontal ligament formation, etc.). Although all of the following parameters may be submitted, only data from histological sections will be needed for endosseous implants with 510(k) clearance and about which specific claims of tissue response are made. The endosseous implants that have not been found substantially equivalent should submit all of the listed parameters.

Animal studies should incorporate a statistically significant number of animals and implants. A minimum study period of one year is needed for each animal. An animal study should be provided for each type (blade, cylindrical, screw, etc.) of endosseous implant manufactured. The parameters listed should be measured and/or observed, at a minimum at 2-week, 1-month, 2-month, 3-month, 6-month, and 1-year postoperatively.

a) Decalcified and undecalcified bone histological specimens - These specimens should document the cellular activity (osteogenesis), bone-implant interface, vascularization, gingival attachment, foreign body reaction, and inflammation (if present).

b) Periapical and panoramic radiographs - These radiographs should be standardized to ascertain bone resorption quantitatively. Pre-surgical radiographs should be taken, in addition to the above postoperative evaluation (specified in VI.A.1.). The 2-week, 1-month, 2-month radiographs may be eliminated to reduce any potential affect of x-rays on bone growth.

c) Mobility - The following categories should be used to quantify the observations made.

(1) No visual movement upon palpation
(2) Visually mobile but less than .5mm total buccolingual movement
(3) Greater than .5mm but less than 1mm total buccolingual movement
(4) Greater than 1mm total buccolingual movement

In addition, rotational movement should be monitored. This parameter should be measured in degree of rotation (approximate). It is recognized that this measurement is approximate and may not apply to all implant applications (i.e., fixed prosthesis). In addition, mobility measurements in two-stage implant systems should begin at the point when the abutment is to be attached.

d) Gingival Health - Quantify the observations by using the following categories. Gingival hyperplasia and regression can be measured by recording the distance between the most coronal aspect of the implant and gingiva.

(1) Inflammation

i) No inflammation
ii) Marginal inflammation of less than 2mm
iii) Inflammation greater than 2mm but less than 4mm
iv) Inflammation greater than 4mm and/or fistula
v) Bleeding upon probing
vi) Spontaneous bleeding
vii) Presence or absence of suppuration

(2) Gingival hyperplasia

i) None
ii) Less than 1mm
iii) 1 - 3mm
iv) Greater than 3mm

(3) Gingival regression

i) None
ii) Less than 1mm
iii) 1 - 3mm
iv) Greater than 3mm

e) Pocket Depth - actual measurements

(buccallingual, mesiodistal, and axial) should be taken

f) Attachment levels - measured from the most coronal aspect of the implant to the bottom of the pocket (buccallingual, mesiodistal, and axial)

2. Biocompatibility

Refer to the "Tripartite Biocompatibility Guidance for Medical Devices". Special consideration should be given to irritation tests, sensitization assays, cytotoxicity, acute systemic toxicity, pyrogenicity (material-mediated), subchronic toxicity, chronic toxicity and carcinogenesis bioassay.

3. Wear

a) The rationale for and the results of all engineering tests performed and reported relative to material properties and device design

b) The physical properties of the implanted devices after prolonged exposure to the biological environment. This would include engineering testing detailed in IV. B. 6 & 7. Any observed corrosion should also be reported.

c) The system reliability should be assessed both predictively and retrospectively. Predictive techniques include tolerance analysis, fault tree analysis, failure modes and effects analysis (FMEA) and mean time between failure (MTBF) prediction. Retrospective techniques include demonstrations of reliability through environmental and accelerated stress tests as well as FMEA and fault tree analyses of actual in-vivo and in-vitro failures. Design revisions that result from the system reliability analyses should be discussed. Particular attention should be given to failures that could injure the patient, create discomfort require corrective surgery, or cause irreversible soft or hard tissue loss.

(1) A discussion of the techniques for predicting and testing the in-vivo reliability and stability of implanted components should be included. In this regard, the sponsor should set forth the rationale and test data that support his selection of materials, surface preparation, method of interlocking

individual components of the implant system, and coatings employed to prevent or retard deterioration of the implant, i.e., such as corrosion, fracture, and fatigue.

(2) To summarize, the reliability analysis should address predictive analyses as described above with special emphasis on methods and data used in FMEA and tolerance analysis and on determination of FMEA categories, and retrospective methods as described above with special emphasis on methods and data used to evaluate in-vitro reliability of implanted components and on environmental test methods and results for nonimplanted components

4. Shelf life

B. Clinical Investigations

The clinical investigation should include a well controlled clinical trial designed to demonstrate the safety and effectiveness of the implant as described in the "Indications for Use". At least two independent controlled clinical studies, each consisting of a minimum of 50 patients, should be conducted. The study period should be a minimum of three years, with the implant under load conditions, and a two year postmarket surveillance (after the PMA is approved) surveillance. These studies should monitor patients closely with 100 percent follow-up or with a detailed explanation required for any loss of follow-up. The final number of patients in each study followed for the entire three year period should represent a statistically significant study. The studies should be conducted by qualified investigators experienced in implant dentistry, clinical research design, and data analysis.

The data derived from these investigations should meet the definition of valid scientific data as defined in 21 CFR 860.7. The studies should be specifically designed to demonstrate that the implant is effective in a particular site in the alveolar ridge (i.e., mandible vs. maxilla).

Investigations of this nature are to be conducted in such a way that the participating subjects or patients are exposed to the least possible risk consistent with the anticipated benefits. Patients must be advised that an investigational device is being used and informed consent must be executed by the patient (if no 510(k) has been found substantially equivalent for the specific implant being studied). Patient informed consent, when

applicable, should follow FDA Guidelines on Informed Consent - 21 CFR Part 50. The FDA Guidelines on Informed Consent do not apply for endosseous implant manufacturers that have completed a premarket notification on their particular implant and have been found substantially equivalent to pre-Amendments endosseous implants.

The final prototype of the device should be used in all cases. A clinical study must be repeated each time a device is changed significantly (i.e., change would alter safety and/or effectiveness of device) or a new prototype developed, unless waived by the review committee.

1. Clinical protocols:

   a) Preimplant assessment

      (1) Describe the general health of the patient

      (2) Detail the location of the intended site for implantation (i.e., where on the mandible or maxilla). Describe the pathological condition (i.e., infection, bleeding, inflammation, etc.) of the intended surgical area and surrounding areas (i.e., periodontium, oral cavity, bone, etc.)

      (3) Determine the condition of the opposing teeth. Describe any abnormal occlusion that the implant might encounter.

      (4) Radiographs should be used to quantify the ridge height and width of the supporting bone and locate major anatomical features. These radiographs must be standardized so that each subsequent radiograph can be directly compared. This procedure should be used in postimplant assessment as well. Other methods for assessing the bone width for the maxilla may be necessary.

         a) Periapical or panoramic

         b) Occlusal

         c) Cephalometric

         d) CAT Scans

      (5) Describe the rationale for determining

the size and type of implant to be used

(6) Describe how the patient will be counseled on the specific types of oral hygiene that will be necessary to maintain the implant.

b) Postimplant assessment

(1) Length (three years, with the implant under load conditions, with additional two years postmarket (after PMA is approved)) and frequency (postsurgical, 2-week, 1-month, 3-month, 6-month, 12-month, 18-month, 2-year, and 3-year postoperative minimum) of evaluation. Include the time elapsed between each stage of the implantation (i.e. time between surgical preparation, insertion of the abutment, and when implant is first subjected to forces of occlusion). Detail any medication that the patient is taking during the clinical trials (this would include the postmarket surveillance period). The following parameters and/or observations should be taken during each evaluation.

(a) Radiographs as described in the preimplant assessment should be used. Radiographs may not be required at each postimplant assessment.

(b) Gingival health as described in the nonclinical section

(c) Mobility as described in the nonclinical section

(d) Pocket depth as described in the nonclinical section

(e) Attachment level as described in the nonclinical section

(f) Complications that are encountered and the times at which the complications occurred. These would include, but not be limited to, permanent anesthesia or paresthesia, mandibular fracture, loss of mandibular or maxillary alveolar ridge, osteomyelitis, oro-antral or

oro-nasal fistula, adjacent teeth affected adversely by implant, pain for more than one month after insertion, local or systemic infection secondary to the implant.

(g) Oral hygiene

2. Number and experience of investigators

   a. The investigators should be knowledgeable in the area of implant dentistry, clinical research design, and data analysis.

   b. A minimum of two studies, each conducted by an independent investigator, should be performed. Each study should be performed at separate locations.

3. Study population, including the distribution of such relevant variables as

   a) Concomitant therapy and special education, e.g., oral hygiene

   b) Numbers of patients in experimental and, when used, control groups

   c) Age and gender distribution

   d) Single tooth, fixed partial prosthesis or fixed complete prosthesis or overdentures

   e) Prosthetic variables

      (1) Maxillomandibular jaw relationships
      (2) Prosthetic design of abutment
      (3) Replacement tooth material (e.g., porcelain acrylic, metal, etc.)
      (4) Dentition matrix
      (5) Occlusal scheme

4. Subject selection criteria (including a description of and rationale for, any deviation from the patient inclusion criteria). These criteria should include the amount of bone needed to support the implant used and the minimum age of the patient.

5. Adverse reactions and complications (including a description of each individual adverse reaction and/or complication)

6. Any additional safety and effectiveness data collected during the study

7. The number of patients discontinued, the rationale for discontinuation and time of discontinuation

9. Patient complaints

10. Device failures and replacements (including a detailed and complete failure analysis report for each device failure)

11. Tabulations of data from all individual subject report forms

12. Copies of subject report forms for each subject who did not complete the investigation

13. Results of statistical analyses of the clinical investigations (including the statistical methodology and rationale for each test and/or references and/or formulas for each methodology and a description of and explanation for any deviations from the methodology)

    a) In order to determine the effectiveness of the device this study should include a statistically valid number of patients and complete follow-up at regular intervals.

    b) The analysis of the data should be done by the success or failure rate and the complication rate. The time-specific cumulative failure rate and complication rate can be calculated by statistical survival analysis, if appropriate.

14. Contraindications and precautions

15. Any other appropriate information such as

    a) A summary table specifying duration of follow-up for each subject in the investigation

    b) A statement as to why a study was discontinued, if it was, or a statement that it is continuing, if such is the case

    c) The methods used to eliminate bias on the part of the subjects or investigators

d) Previous clinical experience with the implant that was conducted outside the three year controlled clinical studies. This would not be considered part of the required three year controlled clinical studies.

16. Was this investigation conducted under an IDE and in compliance with 21 CFR Part 812, Investigational Device Exemptions? This would only be applicable to manufacturers that did not go through the FDA premarket notification process (510(k)).

VII. Reports and Other Information

A. Bibliography of all published reports not submitted under 21 CFR 814.20(b)(6), whether adverse or supportive, that concern the safety and effectiveness of the device

B. Identification, discussion, and analysis of any other data, information or report (foreign or domestic) relevant to an evaluation of the safety and effectiveness of the device

C. Copies of any published report or unpublished information if requested by FDA or an FDA advisory committee

VIII. Samples

Only if requested by FDA, one or more samples of the device

IX. Labeling

A. Submit copies of all proposed labeling. Include instructions for implantation and any information, literature, or advertising that constitutes labeling under section 201(m) of the Federal Food, Drug, and Cosmetic Act.

B. Labeling for the device (Draft labeling should be prepared using the following format, order, and section headings: DESCRIPTION, INDICATIONS AND USAGE, INFORMATION FOR USE, CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, ADVERSE EFFECTS, and where necessary, REFERENCES. If there are no known contraindications, warnings, precautions, or adverse effects, the labeling should indicate "none" or "none known" under each of the headings. The labeling must state whether the device is to be restricted (21 CFR 801 and 899).

C. Surgical and prosthetics manual

D. Patient information

F. Promotional material, written or otherwise

X. Environmental Assessment

A. If claiming a catergorical exclusion, information to justify the exclusion

B. An environmental assessment

XI. Appendix

A. Patient informed consent (This would be applicable only if manufacturer did not go through the FDA premarket notification process (510(k))for their respective implant) must be consistent with 21 CFR Part 50 and should include

1. A statement describing the device and its functions

2. The benefits and risks of other approved dental implant methods and of other alternative dental procedures

3. The risks, as well as the benefits, of dental implants in general and the risks and/or requirements of the particular type of dental implant under evaluation (e.g., resorption of the alveolar ridge, perforation of the maxillary sinus, perforation of labial and lingual plates, infection, exfoliation, taste disturbances, permanent anesthesia or parasthesia, etc.).

4. The possibility that it may be necessary to remove the device and/or utilize other methods in an attempt to regain masticatory function (include risks of revision/reinsertion)

5. Consistent oral hygiene is required to maintain the endosseous implant

6. A stipulation that the patient should also be advised that he or she should remain in communication with the investigator or the manufacturer, with no time limit, in order that the long-term success or failure of the device may be determined and that periodontal and restorative maintenance can be performed.

B. Postmarket surveillance

In order to locate all the dental implants, the manufacturer is to keep records of regional distribution and final distribution (e.g., the individual clinics, or hospitals). In the event of recall or

need to survey the incidence of adverse reactions, manufacturer will provide this information to the In addition, the manufacturers will provide FDA with the total number of implants distributed yearly. The manufacturer should conduct an adverse reaction reporting system in order to actively solicit adverse reactions from health care personnel. The manufacturer should provide educational information for the use of dental implant devices to health care personnel. The patient should also be provided with educational material for maintanence of the dental implant.

Postmarket surveillance may be needed for endosseous implants if less than five years of data is collected from controlled clinical studies.

In addition, the following reasons may warrant further postmarket surveillance:

1. The possiblity of defects in the manufacture of a particular "run" or lot of devices, necessitating the location of patients

2. The possibility that hazards during extended use are discovered at some future date. This could include, but not be limited to, loosening and exfoliation of the implant due to bone resorption and mechanical fatigue and fracture due to corrosion.